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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/466,778	12/20/1999	GREGG A. HASTINGS	PF487	1584

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EXAMINER
MITRA, RITA

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 04/09/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

File Copy

Office Action Summary	Application No.	Applicant(s)	
	09/466,778	HASTINGS ET AL.	
	Examiner	Art Unit	
	Rita Mitra	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 January 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-80* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-80* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

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DETAILED ACTION

Upon further review, the finality of the office action dated October 23, 2001 (paper #16) is withdrawn and the case is reopened for prosecution. Please see notice of references cited (PTO-892) and IDS statement (PTO-1449), which were attached to paper #10 (office action dated April 25, 2001) and paper #16 (office action dated October 23, 2001 respectively.

Status of the Claims

Applicants' amendment and response dated August 3, 2001 (paper #15) to office action dated April 25, 2001 (paper #10) and response dated January 23, 2002 (paper #18) to office action dated October 23, 2001 (paper #16) are acknowledged. Amendments to specification has been entered. Therefore, claims 23-80 are currently pending to which the following grounds for rejection are or remain applicable.

Response to Remarks and Arguments

Withdrawal of Objections

The objection to the specification is withdrawn in light of Applicants' amendments to the specification.

Rejection under 35 U.S.C. 112, second paragraph

The rejection of claims 31, 32, 36, 37, 41-44, 48-51, 55-68 and 72-77 under **35 U.S.C. 112, second paragraph** is withdrawn in light of Applicants' responses (paper #15, page 15 and paper #18, page 6).

Rejection under 35 U.S.C. 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 23-80 remain rejected **under 35 U.S.C. 101** because the claimed polypeptides are not supported by either a specific and substantial asserted utility or a well established utility because the specification fails to assert any utility for the claimed protein.

The amended specification (see paper #15, page 6-7) describes protein set forth in SEQ ID NO: 11 to which the instant invention relates. Specification page 6, lines 22-24 indicates that based on alignment with database submission the claimed polypeptide shares 43% sequence homology with the Mus musculus TSG-6 protein (Fig 8 (SEQ ID NO: 12)). Further (page 7) based on the structural similarity by having hyaluronan binding domain the claimed protein shares some specified activity with this submission.

A sequence identity search for SEQ ID NO: 11 using GenBank database indicates the alignments and percent similarity to sequence cited by the applicants and indicated having similar activity (specification page 16), identified as Accession NO: W84087 (Lee et al., Dec 8, 1998) teach a TSG-6 protein, having 14.1% sequence identity to SEQ ID NO: 11 (see alignment result, A_Geneseq_36 database and US Patent 5,846, 763, Dec 8, 1998, Example V). Lee et al. also teach a TSG 6 protein, having 37% sequence identity to adhesion receptor CD44 (J. of Cell Biology, vol. 116, NO. 2, pp. 545-557, Jan 1992; see Figs. 4, 5 and col.1, page 551).

Further, a sequence identity search for SEQ ID NO: 11 using GenBank database indicates the alignments and percent similarity to sequences, identified as Accession NOs:

Q9NRY3 (Tao et al., Oct 1, 2000) teach a CD44-like precursor FELL, having 93.8% sequence identity to SEQ ID NO: 11 (see alignment result, SPTREMBL_15 database).

Q9UF98 (Blum et al., May I, 2000) teach a hypothetical 115.7 KDA protein fragment, having 80.5% sequence identity to SEQ ID NO: 11 (see alignment result SPTREMBL_15 database).

Thus, the foregoing indicates that the sequence of SEQ ID NO: 11 of the instant application has a lower percentage similarity (14.1%) to the sequence of W84087 (TSG-6 protein) while it has a much higher percentage similarity (93.8% and 80.5%) to Q9NRY3 (CD44

like receptor) and Q9UF98 (a hypothetical protein) respectively. Therefore, only on the basis of some similarity to sequences identified as TSG-6 protein, the protein of SEQ ID NO: 11 cannot be identified as a member of 'TSG-6 (HABP)' family. If the protein has similar activity, it would have indicated close sequence similarity with W84087.

Based on the specification (pages 3, 5, 8, 10, 11), any biological activity of the polypeptide itself has not been provided. However, uses have been provided on pages 9-11 and 210-332 of the specification, but are discussed in the context of being used for further research, but to do what? The function/biological activity of the protein is not per se set forth in the instant specification. One skilled in the art should not have to engage in discovering genomics to learn how to use the invention. This situation requires carrying out future additional research to identify or reasonably confirm a "real world" context of use and therefore do not define specific and substantial utility.

Other activities that the protein may exhibit are listed throughout pages 210-332 of the specification. However, these activities are not demonstrated. In summary, the polypeptides claimed do not have a credible, specific or well-established utility and therefore lacks utility under 35 U.S.C. 101.

Claims 31, 32, 36, 37, 41-44, 48-51, 55-68 and 72-77 are drawn to a protein comprising a fragment of SEQ ID 11. The specification does not describe the functional properties of these protein fragments, and the structural information is limited. While the specification enumerates several known assays for biological activity (p. 215-223), it does not guide the selection of a specific assay that would be used to screen the biological activities of the claimed fragments.

Claim 27 is drawn to a protein comprising the full-length polypeptide encoded by the cDNA contained in ATCC Deposit NO: 203502. It is not clear from the description of the clone (specification pages 15-16) about the protein structure, aside from its full-length amino acid sequence, and/or its function.

Claims 24, 28, 33, 38, 45, 52, 69 and 78 are directed to a protein comprising a heterologous polypeptide sequence. It is not clear from the description of the heterologous proteins (specification page 40) about the protein structure and/or its function.

Claims 25, 29, 34, 39, 46, 53, 70 and 79 are drawn to a composition comprising the protein of SEQ ID NO: 11 and its fragments. Applicants assert on page 337-338 that the composition would be useful in the treatment of conditions associated with disease. Examples of many therapeutic methods have been described in pages 272-332 but the specification does not indicate explicitly the correlation of the role of this composition to a specific disease treatment.

Claims 26, 30, 35, 40, 47, 54, 71 and 80 are drawn to a protein produced by the method comprising expressing the protein by a cell and recovering the protein. Specification on page 56-69 describes the vectors and host cells but does not indicate the function of the expressed protein.

As discussed above, based on the specification it is unclear what activity the claimed proteins or protein fragments possess and therefore unclear how a person having skill in the art might use the claimed polypeptides. It would require undue experimentation for a person having skill in the art to be able to use the claimed polypeptides. It is *a priori* unpredictable based on the instant disclosure what activity the claimed polypeptides possess because no correlation has been made between the claimed polypeptides and a specific activity.

In the instant case, the failure of applicants to specifically identify why the claimed invention is believed to be useful renders the claimed invention deficient under 35 USC 101. No specific biological activity has been identified for the protein set forth in SEQ ID NO: 11 other than the fact that the protein may be hyaluronan-binding protein (p. 3). The person having ordinary skill in the art would not be able to identify any specific activity for the protein comprising or related to SEQ ID NO: 11 based on its structure alone for the reasons set forth above. General statements that a composition has an unspecified biological activity or that do not explain why a composition with that activity is believed to be useful fails to set forth a "specific utility." Brenner v. Manson, 383 US 519, 148 USPQ 689 (Sup. Ct.1966) (general assertion of similarities to known compounds known to be useful without sufficient corresponding explanation why claimed compounds are believed to be similarly useful is insufficient under 35 USC 101).

The rejection has been set forth in the previous office actions. In response, applicants traverse the foregoing rejection and argue (paper #15, pages 10-14) that the claimed invention is

supported by a well-established, credible, specific and substantial utility as the invention features a novel hyaluronan-binding protein BM-HABP (i.e., a novel hyaluronan-binding protein BM-HABP comprising amino acid sequence set forth in SEQ ID NO: 11). Further, applicants assert that on the basis of structural similarity to TSG-6 the protein BM-HABP is identified as a member of 'TSG-6 (HABP)' family. Applicants' arguments are fully considered but not found persuasive because the amendments fail to provide any biological activity of the polypeptides claimed. Applicants indicate at page 12 that Tao et al. (Reference AD) also teach that their protein of Q9NRY3 contains a hyaluronan-binding domain, therefore since BM-HABP is structurally similar to Tao et al.s' protein Applicants assert that BM-HABP of the present invention would have the similar function and utility as in Tao et. al.s' protein. The argument is not persuasive because Applicants have not provided any activity of the BM-HABP protein which can be correlated with the activity of Tao et al.s' protein. The prior art (Reference AD) does not provide a support in establishing utility of the claimed invention. Therefore, the claimed invention is not supported by a well established, credible, specific and substantial asserted utility.

In regard to the rejection of the claims under 35 U.S.C. 101, Applicants argue (paper #18, page 3) that the burden is on the Examiner to establish that the asserted utility is not credible. Applicants' arguments have been noted but not found persuasive. As stated in previous office actions that because the claimed invention is not supported by a specific asserted utility for the reasons that the specification fails to disclose any activity for the claimed polynucleotides or the encoded proteins, credibility can not be assessed. Applicants also point out at page 4, lines 1-5 that the Examiner has presented no evidence to disprove Applicants' asserted utilities for BM-HABP. It has been stated in previous office action and restated above that the sequence of SEQ ID NO: 11 of the instant application has a lower percentage similarity (14.1%) to the sequence of W84087 (TSG-6 protein) while it has a much higher percentage similarity (93.8% and 80.5%) to Q9NRY3 (CD44 like receptor) and Q9UF98 (a hypothetical protein) respectively. Therefore, only on the basis of some similarity to sequences identified as TSG-6 protein, the protein of SEQ ID NO: 11 cannot be identified as a member of 'TSG-6 (HABP)' family. If the protein has similar activity, it would have indicated close sequence similarity with W84087. Applicants have not provided any activity of the BM-HABP protein which can be correlated with the activity of

Q9NRY3 or W84087 protein. The prior art Q9NRY3 (Tao et al. Reference AD) does not provide a support in establishing utility of the claimed invention just because the protein of Tao and the protein of instant application contain a hyaluronan-binding domain. Therefore, the claimed invention is not supported by a well established, credible, specific and substantial asserted utility.

In response to Applicants' citation of MPEP 2107.02 (III)(A) at 2100-39 and also *In re Langer* the Applicants have quoted " an applicant's assertion of utility creates a presumption of utility that will be sufficient to satisfy the utility requirement of 35 USC 101." However, Applicants should note that further it is stated in *In re Langer* that " unless there is a reason for one skilled in the art to question the objective truth of the statement of utility or its scope." (see MPEP at 2100-30 and *In re Langer*). Therefore, Langer is unpersuasive because in the instant case Applicants' assertion of utility is on the basis of structural similarity with TSG-6 (Lee), which has only 14.1% sequence homology, while protein of Tao has 93.8% sequence identity with the protein claimed. Therefore, this reason is sufficient for one skilled in the art to question the objective truth of the statement of utility.

In response to Applicants' citation of *In re Cortright* the court indicated that the Board reversed the section 101 rejection because the Examiner did not set out sufficient reasons for finding Cortright's statements of utility incredible. It should be noted here that Cortright is unpersuasive because in the instant case sufficient reasons and factual data have been provided in support of the finding of a lack of a specific and substantial or well established utility.

In response to Applicants' citation of *In re Brana* the court indicated that the..."evidence that compounds within scope of claims, and other structurally similar compounds, are effective as chemotherapeutic agents in animals would be sufficient to convince one skilled in art of asserted utility"...Applicants should note that Brana has no correlation with the reasons given for 101 rejection because in the instant case Applicants' assertion of utility is on the basis of structural similarity with TSG-6 (Lee), which has only 14.1% sequence homology. Applicants fail to describe any activity that would correlate with the protein of Tao, which has 93.8% sequence identity with the protein claimed. Therefore, how it would be sufficient to convince one skilled in art of asserted utility?

Rejection under 35 U.S.C. 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 23-80 remain rejected under **35 U.S.C. 112, first paragraph**. Specifically, since the claimed invention is not supported by either a specific and substantial asserted or well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention so that it would operate as intended due to the absence of appropriate description of same in the application as filed. In regard to the comments in the response Applicants remark on page 15 (paper #15) that the specification teaches the use of the polypeptide fragments as immunogens to raise antibodies, which does not require biological activity. Applicants' arguments are not persuasive because without knowing the activity of the antibodies raised from the polypeptide fragments how one can practice the invention without knowing the function of those antibodies, which would be, raised against the claimed polypeptide fragments. Applicants also argue at page 6, lines 8-10 in paper #18 that the instant claims are not limited to biologically active fragments, or to fragments with only particular activities. The argument is not found persuasive because the fragments and sequences having less than 100% identity to SEQ ID NO: 11 should have specific activity such that the fragments or other proteins meeting the structural requirement of the claims will be known by their functional requirements. Therefore 112, first paragraph rejection remains.

Conclusion

Claims 23-80 are rejected.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rita Mitra whose telephone number is (703) 605-1211. The Examiner can normally be reached from 9:30 a.m. to 6:30 p.m. on weekdays. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Christopher

Low, can be reached at (703) 308-2923. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in he Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center number is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Rita Mitra, Ph.D.
April 2, 2003

Christopher S. F. Low

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